PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.08.2000

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
01528.001	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/11977	28/05/1999	29/05/1998

Applicant
CHIRON CORPORATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Digiusto, M Tel.+49 89 2399-8162

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
01528.001		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/11977	28/05/1999	29/05/1998

International Patent Classification (IPC) or national classification and IPC
A61K39/095

Applicant
CHIRON CORPORATION et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20/12/1999	23.08.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bradbrook, D Telephone No. +49 89 2399 7413

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/11977

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-10 as originally filed

Claims, No.:

1-16 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 8-14,16 for IA.

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 4,11
	No:	Claims 1-3,5-10,12-16
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-16
Industrial applicability (IA)	Yes:	Claims 1-7,15
	No:	Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section III

1. Non establishment of opinion

Claims 8-14 and 16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V

2. Reference is made to the following documents:

D1: WO-A-90 06696 (Praxis Biologics Inc. and Rijkinsinstituut v. Volksgez.; 28.06.90);
D2: Liebermann et al., JAMA, Vol.275, pp.1499-1503 (1996);
D3: Product information from S.C.S. Farmacia Manes, Argentina;
D4: Debbag et al., Clin.Infect.Dis., Vol.21, p.790, Abstr.A420 (1995);
D5: Granhoff et al., Infection and Immunity, Vol.65, pp.1710-1715 (1997).

D1 discloses vaccine formulations comprising outer-membrane vesicles, Class 1 outer membrane proteins (OMPs), or epitope-containing fragments or oligopeptides thereof, from Neisseria meningitidis. Effective vaccines should comprise OMPs from N. meningitidis group B, and may additionally contain meningococci A and C polysaccharides, preferably coupled to a protein or polypeptide carrier such as a nontoxic mutant bacterial toxin (CRM); CRM197 is cited as the carrier protein in claim 41. The vaccine may also contain an adsorbant such as alum. See "Detailed description", p.7-p.10, para.1.

D2 concerns a vaccine comprising N. meningitidis groups A and C oligosaccharide-protein conjugates (see abstract).

D3 gives information on the VA-MENGOC-BC vaccine, which comprises polysaccharides from N. meningitidis group C conjugated to outer membrane proteins from group B (see "Composición").

D4 concerns an evaluation of adverse reactions to the VA MENGOC-BC vaccine, and is cited to show that said vaccine was in use before the priority date of the present application.

D5 discloses enhanced antibody responses when using MF59 adjuvant with N. meningitidis and Haemophilus influenzae conjugate vaccines (abstract).

3. Novelty (Article 33(2) PCT)

a. D1 seems to anticipate the subject-matter of independent claims 1, 8, 15 and 16, as well as dependent claims 2, 3, 5-7, 9, 10 and 12-14. Therefore, these claims are not considered to be novel over D1.

b. Inasmuch as claim 1 does not exclude an embodiment wherein the NmB outer membrane protein is the first carrier to which the NmC oligosaccharide is conjugated, this composition is not distinguishable from that with the VA-MENGOC-BC vaccine, described in D3. Therefore, claims 1-3, 6-10, and 13-16 appear not to be novel over D3.

c. In claims 4 and 11, the carrier protein is defined as CRM 197. Although this same carrier protein is also used in D1, the context of its use is very specific (see claim 41) and is not considered to apply necessarily to the compositions disclosed therein in a general manner. Thus, claims 4 and 11 would appear to be novel.

4. Inventive step (Article 33(3) PCT)

a. Claims 4 and 11 are not considered to be inventive: in D1, CRMs as a group are proposed as carrier proteins, and CRM197 in particular is preferred in one particular embodiment (claim 41). The skilled person would readily understand that CRM197 is generally applicable as a carrier protein for the vaccines in D1 and would require no inventive skill in using it as such. Moreover, polysaccharides from N. meningitidis groups A and C were coupled to the carrier CRM197 in a vaccine in D2 (p.1500, col.2: "Vaccines"). Thus, said claims do not appear to be inventive over D1 alone, or in combination with D2.

b. It is noted that the advantageous use of adjuvant MF59 with meningococcal vaccines is disclosed in D5.

5. Industrial applicability (Article 33(4) PCT)

For the assessment of the present claims 8-14 and 16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VII

6. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 and D5 is not mentioned in the description, nor are these documents identified therein.

Section VIII

7. The following objections arise under Article 6 PCT:

a. Abbreviations in the claims, such as NmB and NmC, should have been written out in full, at least in the independent claims (PCT Guidelines C-III 4.2).

b. Claim 5 should have read "The immunogenic composition of claim 1 **wherein** ...".

c. The vague and imprecise statement in the description, p.6, l.3-4, referring to the "spirit" of the invention, implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity when used to interpret them (see also PCT Guidelines, C-III, 4.3a).